Remarks

The foregoing amendments to the claims are believed to place the claims into condition for immediate allowance or into better condition for consideration on appeal. Moreover, the amendments do not raise new issues for consideration by the Examiner. Entry of the present amendment and reconsideration of this application is respectfully requested.

Upon entry of the foregoing amendment, claims 1, 3, 4, 6, 7, 10, and 11 are pending in the application, with 1 and 6 being the independent claims. Claims 1, 3, 6, and 7 are sought to be amended. Support for the amendments is found in the claims as originally filed. Claims 5, 8, and 9 are sought to be canceled without prejudice to or disclaimer of the subject matter therein. New claims 10 and 11 are sought to be added. Support for the new claims is found in claims 3 and 4 as originally filed. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

Allowable Subject Matter

Applicants appreciate the Examiner's acknowledgment that claim 6 would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. (Office Action, page 10). Applicants have amended

claim 6 to independent form and have added new claims 10 and 11 that depend from claim 6. Applicants assert that claims 6, 10, and 11 should be found to be allowable.

Rejections under 35 U.S.C. § 103(a)

Claims 1, 3, 7, and 8 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Mandecki *et al.* (U.S. Patent No. 6,046,003) in view of Akram *et al.* (U.S. Patent No. 6,250,192). (Office Action, page 3). Applicants respectfully traverse this rejection.

The Examiner is of the opinion that:

> Mandecki teaches a method for producing a labeled nucleic acid (e.g., fluorescently-labeled target DNA bound to probe attached to the surface of the transponder), wherein the method comprises binding the nucleic acid (e.g., oligonucleotides) to a large scale integrated circuit (e.g., solid phase particles having a transponder associated with each particle), and recording specific information (e.g., the sequence of the oligonucleotide) on the large scale integrated circuit (column 1, lines 55-column 2, line 6, column 17, lines 28-44).
>
> Mandecki expressly exemplifies the situation where double stranded nucleic acid is bound to the transponder (see figure 1, where the nucleic acid shown in clearly double stranded). . . .
>
> Mandecki does not teach the use of integrated circuits with 320 million bits of memory (equivalent to 40 million bytes or 40 megabytes of memory).
>
> Akram teaches the use of RFID integrated circuits with a capacity of 64 megabytes (see column 2, lines 1-15, especially line 9).
>
> It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to modify the Mandecki device to use large integrated circuits since Mandecki expressly notes "The present invention can be practiced with different transponders,

> which might be of different dimensions and have different electronic memory capacity (see column 5, lines 57-60).

(Office Action, pages 3-4). Applicants respectfully disagree.

Claim 8 has been canceled, rendering that portion of the rejection moot. The claims as amended are directed to a method for producing a labeled nucleic acid, wherein the nucleic acid is circular, the method comprising binding the nucleic acid to a LSI that comprises more than 320 million bits of memory, wherein specific information characteristic to the nucleic acid is recorded on the LSI.

In contrast, Mandecki describes a method for determining the sequence of target nucleic acids in which oligonucleotide probes attached to transponders are allowed to interact with the target nucleic acids and the binding between the probes and the targets is detected (sequencing by hybridization). This method requires hybridization between the probes and the target nucleic acids. Thus, the probes immobilized on the transponders must be in a form suitable for hybridization. Mandecki states that "[i]t is preferred that the immobilized nucleic acids are single-stranded (col. 3, lines 27-29). Throughout the patent, Mandecki refers only to the use of oligonucleotides as probes (*e.g.*, col. 3, lines 36-54; col. 4, line 67 to col. 5, line 2; col. 7, lines 52-56). Mandecki fails to teach how to use circular nucleic acids in the technique of sequencing by hybridization, fails to teach how to bind a circular nucleic acid to a transponder so that it can be used for sequencing, and fails to teach any other use for a circular nucleic acid bound to a transponder. Thus, it could not have been obvious to one of ordinary skill in the art to modify the method of Mandecki to produce transponder-linked probes that are circular. One would not have been motivated to modify Mandecki in this manner as one would not expect circular probes to work in the described sequencing method.

Furthermore, the Examiner admits that Mandecki does not teach the use of integrated circuits with 320 million bits of memory. The Examiner does point out that Mandecki notes "the present invention can be practiced with different transponders, which might be of different dimensions and have different electronic memory capacity" (col. 5, lines 57-60). The Examiner asserts that Akram *et al.* teach the use of RFID (radio-frequency ID) integrated circuits with a capacity of 64 megabytes and that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify the Mandecki device to use larger integrated circuits.

Applicants respectfully disagree. Akram *et al.* simply do not teach an RFID integrated circuit with a capacity of 64 megabytes as Akram *et al.* disclose RFIDs and 64 megabyte DRAMs as parts of separate and unrelated embodiments. The Examiner cites *KSR International Co. v. Teleflex Inc.*, 82 U.S.P.Q.2d 1385, 1396 (2007) to imply it would be obvious to combine the LSI of Mandecki with the use of a larger size memory as discussed by Akram *et al.* (Office Action, page 11). This is a misapplication of *KSR*. *KSR* suggests that it may be obvious to combine elements from different fields of endeavor if there would be a predictable improvement. Here, the Examiner's combination of references doesn't just require combining an embodiment from Akram *et al.* with an embodiment from Mandecki. One of ordinary skill in the art would first have to combine two elements disclosed by Akram *et al.* (an RFID and a 64 megabyte DRAM) and then combine that combination with a circular nucleic acid not even taught by Mandecki, bound to a transponder, to arrive at the claimed invention. *KSR* is not applicable to the present rejection as not all of the elements of the claimed invention are

in the cited art. The gap between the cited art and the present invention is too great to render the claims obvious to one of ordinary skill in the art.

It is respectfully requested that the rejection of claims 1, 3, 7, and 8 as being obvious over Mandecki in view of Akram *et al.* be withdrawn.

Claims 1, 3, 5, 7, and 9 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Nova *et al.* (U.S. Patent No. 5,741,462) in view of Akram *et al.* (Office Action, page 5). Applicants respectfully traverse this rejection.

The Examiner is of the opinion that:

> Nova teaches a method for producing a labeled protein or gene (see abstract), wherein the method comprises binding the protein to a large scale integrated circuit (see column 29, line 45 to column 30, line 14, where antibodies are bound to the integrated circuit), and recording specific information that is characteristic of the peptide (see column 29, lines 50-55 where each antibody "is given a specific identification tag") on the large scale integrated circuit (see columns 29 and 30). . . .
>
> Nova does not teach the use of integrated circuits with 320 million bits of memory (equivalent to 40 million bytes or 40 megabytes of memory).
>
> Akram teaches the use of RFID integrated circuits with a capacity of 64 megabytes (see column 2, lines 1-15, especially line 9.
>
> It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to modify the Nova device to use larger integrated circuits since Nova expressly notes "Based on current semiconductor integrated circuit fabrication process capabilities, in a preferred embodiment the finished chip on which all of the listed components are integrated is on the order of 1 mm.times.1 mm [.about.40 mils.times.40 mils], with a memory capacity of 1024 bits. Greater memory capacity, where needed, and smaller chips, however, will be preferred. The chip may be larger to accommodate more memory if desired, or may be smaller as design rules permit smaller transistors and higher device densities (see column 21, lines 8-16).

(Office Action, pages 6-7). Applicants respectfully disagree.

Claims 5 and 9 has been canceled, rendering that portion of the rejection moot. The claims as amended are directed to a method for producing a labeled nucleic acid, wherein the nucleic acid is circular, the method comprising binding the nucleic acid to a LSI that comprises more than 320 million bits of memory, wherein specific information characteristic to the nucleic acid is recorded on the LSI. In contrast, Nova *et al.* describe matrices with memories that may be bound to a biological molecule. Nova *et al.* mention that the matrices may be used for techniques such as nucleic acid synthesis, nucleic acid amplification, and nucleic acid sequencing (column 5, lines 53-61). However, Nova *et al.* fail to teach how to use circular nucleic acids in any of these techniques, fail to teach how to bind a circular nucleic acid to a matrix so that it can be used for these techniques, and fail to teach any other use for a circular nucleic acid bound to a matrix.

The Examiner admits that Nova *et al.* do not teach the use of integrated circuits with 320 million bits of memory. The Examiner does point out that Nova *et al.* note "[g]reater memory capacity, where needed, and smaller chips, however, will be preferred" and "[t]he chip may be larger to accommodate more memory if desired, or may be smaller as design rules permit smaller transistors and higher device densities" (col. 21, lines 8-16). The Examiner asserts that Akram *et al.* teach the use of RFID (radio-frequency ID) integrated circuits with a capacity of 64 megabytes and that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify the Nova *et al.* device to use larger integrated circuits.

Applicants respectfully disagree. Akram *et al.* simply do not teach an RFID integrated circuit with a capacity of 64 megabytes as Akram et al. disclose RFIDs and 64 megabyte DRAMs as parts of separate and unrelated embodiments. The Examiner cites *KSR* to imply it would be obvious to combine the matrix of Nova *et al.* with the use of a larger size memory as discussed by Akram *et al.* (Office Action, page 11). This is a misapplication of *KSR*. *KSR* suggests that it may be obvious to combine elements from different fields of endeavor if there would be a predictable improvement. Here, the Examiner's combination of references doesn't just require combining an embodiment from Akram *et al.* with an embodiment from Nova *et al.* One of ordinary skill in the art would first have to combine two elements disclosed by Akram *et al.* (an RFID and a 64 megabyte DRAM) and then combine that combination with a circular nucleic acid not even taught by Mandecki, bound to a transponder, to arrive at the claimed invention. *KSR* is not applicable to the present rejection as not all of the elements of the claimed invention are in the cited art. The gap between the cited art and the present invention is too great to render the claims obvious to one of ordinary skill in the art.

It is respectfully requested that the rejection of claims 1, 3, 5, 7, and 9 as being obvious over Nova *et al.* in view of Akram *et al.* be withdrawn.

Claim 4 has been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Mandecki in view of Akram *et al.* and further in view of Stavrianopoulos *et al.* (U.S. Patent No. 4,994,373). (Office Action, page 8). Applicants respectfully traverse this rejection.

The Examiner is of the opinion that:

> Mandecki in view of Akram teach the limitations of claims 1, 3 and 7 as discussed above.

> Mandecki does not teach the specific substrates of claim 4.
>
> Stavrianopoulos teaches attachment of nucleic acids to plastic matrices (see column 12, lines 5-15, for example).
>
> It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the epoxy resin of Stavrianopoulos to attach the nucleic acids of Mandecki in view of Akram since Stavrianopoulos notes "An improved capability for fixing or immobilization of DNA to non-porous siliceous solid supports, such as glass and plastic, is also provided by treatment with a coating of an epoxy resin. (see column 12, lines 5-15)".

(Office Action, page 8). Applicants respectfully disagree.

As discussed above, Mandecki in view of Akram *et al.* does not teach a method for producing a labeled circular nucleic acid, comprising binding the circular nucleic acid to an LSI that comprises more than 320 million bits of memory. The teachings of Stavrianopoulos *et al.* do not cure the deficiencies of Mandecki and Akram *et al.* Stavrianopoulos *et al.* simply teach a method for using a probe that has been labeled with an enzyme or such to quantitatively detect target polynucleotide within a sample, and do not teach or suggest using "information" as a label. Stavrianopoulos *et al.* say nothing about the use of LSIs. Thus, even if the teachings of Mandecki, Akram *et al.*, and Stavrianopoulos *et al.* were combined, one of ordinary skill in the art could not have arrived at the currently claimed method.

It is respectfully requested that the rejection of claim 4 as being obvious over Mandecki in view of Akram *et al.* and further in view of Stavrianopoulos be withdrawn.

Claim 4 has been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Nova *et al.* in view of Akram *et al.* and further in view of

Stavrianopoulos *et al.* (Office Action, page 9). Applicants respectfully traverse this rejection.

The Examiner is of the opinion that:

> Nova in view of Akram teach the limitations of claims 1, 3, 5, 7 and 9 as discussed above.
>
> Nova teaches a variety of synthetic plastic matrices as substrates at column 17, but Nova does not teach the specific substrates of claim 4.
>
> Stavrianopoulos teaches attachment of nucleic acids to plastic matrices such as those of Nova using epoxy resin (see column 12, lines 5-15, for example).
>
> It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the epoxy resin of Stavrianopoulos to attach the nucleic acids or proteins of Nova in view of Akram since Stavrianopoulos notes "An improved capability for fixing or immobilization of DNA to non-porous siliceous solid supports, such as glass and plastic, is also provided by treatment with a coating of an epoxy resin. (see column 12, lines 5-15)".

(Office Action, page 9). Applicants respectfully disagree.

As discussed above, Nova *et al.* in view of Akram *et al.* does not teach a method for producing a labeled circular nucleic acid, comprising binding the labeled circular nucleic acid to an LSI that comprises more than 320 million bits of memory. The teachings of Stavrianopoulos *et al.* do not cure the deficiencies of Nova *et al.* and Akram *et al.* Stavrianopoulos *et al.* simply teach a method for using a probe that has been labeled with an enzyme or such to quantitatively detect target polynucleotide within a sample, and do not teach or suggest using "information" as a label. Stavrianopoulos *et al.* say nothing about the use of LSIs. Thus, even if the teachings of Nova *et al.*, Akram *et al.*, and Stavrianopoulos *et al.* were combined, one of ordinary skill in the art could not have arrived at the currently claimed method.

It is respectfully requested that the rejection of claim 4 as being obvious over Nova *et al.* in view of Akram *et al.* and further in view of Stavrianopoulos be withdrawn.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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Date: October 31, 2007

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